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Published in:
British Journal of Dermatology

DOI:
10.1111/bjd.15016

Publication date:
2017

Document Version
Peer reviewed version

Received Date : 15-Jul-2016

Revised Date : 15-Aug-2016

Accepted Date : 26-Aug-2016

Article type : Research Letter

Has the epidemic of allergic contact dermatitis due to Methylisothiazolinone reached its peak?

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Funding: None

Conflicts of interest: None declared

SIR,

Methylisothiazolinone (MI) is a preservative used in many household and industrial products. There has been an unprecedented global rise in allergic contact dermatitis (ACD) from its presence in personal care products (PCPs).

In 2005 changes to EU legislation allowed MI, used in combination with methylchloroisothiazolinone (MCI), to be used at concentrations of up to 100ppm, 25 times higher than previously permitted. MI was also permitted to be used alone, whereas previously it was only used in combination with MCI in a 3:1 mix.[1]This resulted in the chain of events that led to the current MI allergy epidemic.By 2010, the first case series of ACD to MI as a cosmetic allergen was published.[2]One year later in 2011 MI was included in the British standard series and European minimal baseline series[3] and by 2013 it was dubbed 'Contact Allergen of the year' by the American Contact Dermatitis Society![4]

In 2014 the British Society for Cutaneous Allergy described an epidemic of ACD to MI with over 1% of the UK population estimated to be affected. We reported an increase in ACD to MI from 1.7% of those patch tested in 2010 to 11.1% in 2013.[5] We have continued to collect data to provide evidence to governing bodies on sensitization to MI in PCPs and to inform discussion with the cosmetics industry.

From January 1st to June 30th 2014 was collected from 13 centres across the UK and Ireland. Numbers of patients tested to MI, MCI/MI and their results were analysed and compared with the previously collected results from 17 centres from January 2010 to December 2013. In all centres, test agents were applied in Finn Chambers® according to International Contact Dermatitis Research Group guidelines with readings performed on day two and day four.

In total, 3897 patients were patch tested to MI and 2708 patients were patch tested to MCI/MI from January 1st to June 30th 2014. Of these, all were tested to MI 0.2% in aqueous form (aq), (Chemotechnique Diagnostics, Vellinge, Sweden) and MCI/MI 0.01% (aq) or 0.02% (aq) (Trolab, Reinbeck, Germany).

A summary of our data from 2010 to 2014 is shown in table 1 and figure 1a-c. Whilst we had previously reported a steadily increasing incidence of ACD to MI of around 3% per year from 2010 to 2013, in 2014 it appears to have reduced for the first time since we started recording by -0.30%. Although the overall incidence of ACD to MI may have reached a

plateau, it still remains very high, affecting a mean of 10.73% of the patch test clinic population. The incidence of allergy to MCI/MI appears to have mirrored this plateau effect with it reaching 9.60% in 2014 but still yet to decline.

Interestingly, there remains a wide range in the incidence of ACD, figures 1b-c. However 7 centres report a decline in incidence of ACD to MI 2014. Similarly, data for ACD to MCI/MI is varied but does show a trend toward a stabilisation of incidence in 2014, with 6 centres reporting a decline.

Global clinical data on contact sensitization and ACD have established that the current use of MI at 100ppm in PCPs is unsafe, and this should not be disregarded especially when risk assessment based on predictive assays has failed.

Potential reasons for this apparent plateau are twofold: firstly, there is increased awareness of MI allergy amongst the general public due to media coverage, and secondly the cosmetics industry has started to reformulate 'leave on' PCPs which have been filtering into shops over the past 18 months. Whether this has resulted from pressure from the media or the dermatology community remains to be seen.

Although the rate of increase of incidence of allergy to MI in our clinics may be starting to plateau, overall prevalence in the UK is still rising. Slow government and industry response to increasing pressure from clinicians allowed the incidence of ACD to MI to reach 11.03% in 2013 with a current incidence of new allergy diagnosed in 10.73% of those patch tested shows that the MI epidemic is far from resolved. Therefore it is important that dermatologists continue to apply pressure on commercial and governing bodies to ensure that MI is further restricted.

In July 2015 new EU legislation restricted the concentrations of MCI/MI in rinse off products to 15ppm, and banned MI in combination with MCI from leave on products. Similar restrictions are due to come into place for MI use alone.[6]

Completely restricting MI would result in a gradual decline in sensitization as previously seen with methyldibromoglutaronitrile (MDBGN). However, unlike MDBGN, MI has not yet been banned outright and so this trend cannot be predicted. The incidence of ACD to MI is only likely to decline if further changes to legislation are made.

With the European cosmetics industry permitted to use MI alone at a concentration in "rinse off" PCPs at 100ppm, and data suggesting that MI will elicit reactions in MI sensitized individuals at concentrations of 50ppm in rinse off products,[7] a large proportion of the undiagnosed public will suffer from continued episodes of ACD.

Another challenge remains in the use of MI in non-cosmetic products where there is not currently an equivalent legal requirement to report the presence of MI on product labelling, or any restriction on the concentration. Studies have already identified that airborne exposure to paints with MI can trigger ACD in those already sensitised, as well as those with no history of allergy to MI.[8,9] Of note, in some European countries it is required to report the presence of biocides in non-cosmetic products when the concentration exceeds 1%.

In 1997, Alan Dillarstone predicted the regular development of new preservative allergies.[10] This has been reflected clinically where a new wave of sensitization develops as one allergen is phased out and replaced with another. While the current epidemic of sensitization to MI is not over, we must remain vigilant to new cosmetic allergens arising.

In summary, the incidence of ACD to MI in the UK shows a decline for the first time, reaching a peak of 11.03% for ACD to MI and in 2013 and falling to 10.73% in 2014. Further action is needed to accelerate this decline

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Table 1: Number of patients tested with, and number of patients with a positive patch test reaction to, methylchloroisothiazolinone (MCI)/methylisothiazolinone (MI) and MI in participating centres from January 2010 to June 2014

Year	Patients tested to MCI/MI	Patient positive to MCI/MI	% Positive	Patients tested to MI	Patients positive to MI	% Positive
2010	3185	130	4.08	2279	38	1.67
2011	4368	220	5.04	2543	125	4.92
2012	4612	275	5.95	4984	383	7.68
2013	3346	303	9.06	3936	434	11.03
2014*	2708	260	9.60	3897	418	10.73

* Data collected from Jan 1st to June 30th 2014.